The Office Action

Claims 1-26 are pending in the application. Claims 5-8 are withdrawn from consideration due to a restriction election, and claims 1-4 and 9-26 stand rejected under 35 U.S.C. § 112, first paragraph. This rejection is addressed below.

35 U.S.C. § 112, first paragraph

Claims 1-4 and 9-26 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the absence of an *in vivo* working example results in a level of unpredictability which is too high, given that the art does not recognize treatment of any form of congestive heart failure with a neuregulin. Specifically, the Examiner states:

> Since the state of the art does not recognize NRG-1 treatment for any form of congestive heart failure and [Applicants] have no in vivo working examples demonstrating congestive heart failure treatment and the state of the art does not recognize that their in vitro data would reasonably correlate to in vivo treatment, it would be unpredictable and require an undue amount of experimentation to practice [Applicants'] claimed invention. Office Action Paper no. 12, page 2, lines 34-40.

In essence, the Examiner has questioned the likelihood that the invention would be useful, based on a personal interpretation of the experimental results presented in the specification. Such a question is one of utility, not enablement. Applicants disagree with the Examiner's interpretation and provide the following remarks.

Under the case law and its interpretation in the M.P.E.P., a rejection that questions the effectiveness of an invention is properly analyzed as a utility rejection. This procedure has not been followed in the present Office Action. Applicants submit that the 35 U.S.C. § 112, first paragraph, rejection has been

misapplied and the rejection herein is, essentially, a rejection based on the utility requirement of 35 U.S.C. § 101. Accordingly, Applicants direct the Examiner's attention to the Utility Examination Guidelines (Federal Register 66: 1092-1099, 2001; "the Guidelines") and to the M.P.E.P. at §§ 706.03(a)(1) and 2107-2107.02. The Guidelines make it clear that when the efficacy of an invention is questioned, a 35 U.S.C. § 112, first paragraph, rejection may be applied, but only in conjunction with a utility rejection under 35 U.S.C. § 101 (M.P.E.P. § 2107-IV). Consequently, Applicants address the Examiner's rejection with reference to utility requirements.

The analysis to be carried out in determining the appropriateness of a 35 U.S.C. § 101 rejection must include a determination of whether an assertion of utility has been made in Applicants' specification. If an assertion of utility exists, it must be determined whether that utility is specific, substantial, and credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the disclosure and any other evidence of record). Procedurally, the Guidelines make clear that the burden is on the Examiner to provide a detailed explanation for the rejection that is supported, if possible, by documentary evidence indicating why the claimed invention has no specific and substantial credible utility. To quote:

> Office personnel are reminded that they must treat as true any statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. 66 Federal Register 1092, 1098-1099.

If the Examiner determines that the claimed invention has a specific, substantial, and credible utility, neither a 35 U.S.C. § 101 nor a related 35 U.S.C. § 112

rejection may be applied (or, upon rebuttal of the Examiner's position, both rejections must be simultaneously withdrawn).

The Guidelines state that an invention without a specific and substantial utility is one that has a "throwaway," "insubstantial," or "non-specific" utility. With respect to the issue of credibility, the only instances in which the federal courts have found a lack of credible utility were where, "based upon the factual record of the case, it was clear that the invention *could [not] and did not work* as the inventor claimed it did" (M.P.E.P. § 2107, emphasis added). These rare cases have been ones in which the applicant either (a) failed to disclose any utility for the invention or (b) asserted a utility that could be true only "if it violated a scientific principle, such as the second law of thermodynamics, or a law of nature, or was wholly inconsistent with contemporary knowledge in the art" (M.P.E.P. § 2107.01). The present case does not meet *any* of the criteria for a utility rejection.

Applicants clearly state in the specification that the invention features a method for treating or preventing congestive heart failure by administering a neuregulin polypeptide including an epidermal growth factor-like domain. This utility is, on its face, specific, substantial, and credible. The M.P.E.P. states:

> [A] disclosure that identifies a particular biological activity of a compound and an explanation of how that activity can be utilized in a particular therapeutic application of the compound <u>does</u> contain an assertion of specific utility for the invention. See M.P.E.P. 2107.01-II(A).

Applicants have met these requirements and have provided, by the identification of the stimulatory activities exhibited by neuregulins (Specification page 13, lines12-19). A detailed explanation indicating how neuregulins can be administered to a patient for treatment of congestive heart failure using methods known in the art (Specification page 15, lines 17-25, page 16 lines 1-22).

As for the Examiner's assertion that the claims are not enabled absent working examples of treatment of congestive heart failure by neuregulin administration. Applicants point out that the specification clearly describes how to inhibit heart failure using an *in vivo* mouse model of congestive heart failure (aortic stenosis) by administering the neuregulin polypeptides (Specification page 26, lines 1-25 and pages 48-49). Additionally, the specification provides data showing that neuregulins are involved in stimulating compensatory hypertrophic growth in response to physiological stress (Specification pages 32-47). Therefore, one of ordinary skill in the art would have recognized, based on the specification at the time the invention was made, that neuregulin treatment would be useful for preventing, minimizing, or reversing congestive heart disease.

Applicants point out that:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation. Hybritech, Inc. v. Monoclonal Antibodies, Inc. 802 F.2d. 1318 (Fed. Cir. 1985).

Applicants submit that the invention satisfies this test for enablement. First, Applicants used the aortic stenosis model that is well accepted by those skilled in the art as being a suitable experimental example to test mechanism involved in congestive heart failure. By demonstrating that various neuregulin polypeptides inhibit aortic stenonis, Applicants have provided substantial support for neuregulin polypeptide prevention and treatment of congestive heart failure (Specification pages 48-49). Additionally, the administration of polypeptides is a well-established therapy, as evidenced by treatment of diseases with insulin, growth hormone, and erythropoietin, just to name a few. Thus, coupling (a) Applicants' demonstration of the efficacy of neuregulin polypeptides in a well-accepted, *in vivo* disease model and (b) the routine nature of polypeptide therapies, a skilled

artisan would be able to determine the efficacy of a given neuregulin polypeptide within the claims for treatment of congestive heart failure.

Lastly, the relevance of Examiner's statement that "the state of the art does not recognize NRG-1 treatment for any form of congestive heart failure" is puzzling. Use of neuregulins to treat congestive heart failure *is* the present invention. As such, one would not expect to find art detailing this approach prior to Applicants' own specification.

In view of the foregoing remarks, Applicants submit that the bases for the §112, first paragraph, rejection have been successfully addressed, and the invention is enabled. This rejection should be withdrawn.

CONCLUSION

In view of the above remarks, Applicants submit that the claims are in condition for allowance and such action is respectfully requested. Enclosed is a petition to extend the period for replying for three months, to and including July 17, 2001. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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